REMARKS

This paper is submitted in response to an office action dated August 3, 2007. A response is due December 3, 2007, by virtue of the attached petition and fee for a one-month extension of time to respond.

A. Status of the Claims

Claims 24-66 were pending at the time of the office action and stand variously rejected under 35 U.S.C § 112, first paragraph, 35 U.S.C. § 103 (a) and 35 U.S.C. § 102 (b). Applicants traverse the rejection in view of the attached amendment and remarks. Applicants respectfully request reconsideration of the rejection.

B. Rejection of Claims under 35 U.S.C. 112, first paragraph

Claims 24-66 were rejected for recitation of the term "solid preparation" which according to the examiner is not recited in the specification as originally filed. As noted at MPEP 2163.I.B, the applicant is not required to satisfy an *in haec verba* requirement in order to comply with the written description requirement. Rather, if the language of the specification conveys possession of the claimed invention, the written description requirement is satisfied. In the present application, at page12, line 10, it is shown that the methods of the invention are directed to removing degradation products "of glycoalkaloids [that are] in pure or semi-pure crystalline or semi-crystalline form." Applicants submit that a composition that is in a "crystalline or semi-crystalline form" is in fact a solid preparation as opposed to a liquid preparation. However, in order to clarify the record applicants have amended the claim to remove the term "solid preparation" and substituted in its stead the term "crystalline or semi crystalline form." Applicants request that the rejection of the claims based on lack of written description of the term "solid preparation" be withdrawn.

C. Rejection of Claims under 35 U.S.C. 103(a)/102(b)

Claims 24-66 were rejected under 35 U.S.C. 103(a) as allegedly being rendered obvious over Cham et al. 1990 either alone or in various combinations with secondary references. Product by process claims 33-42, 54-58, 60, 65 and 66 were separately rejected under 35 U.S.C. 102(b) as allegedly anticipated by the disclosure of Cham et al.

Applicants traverse the rejections and address the rejections with respect to the method claims and the composition claims separately.

1. Rejection of Claims 24-66 under 35 U.S.C. §103(a)

The primary reference used to reject claims 24-66 is Cham et al. According to the Examiner:

> "Cham discloses a composition comprising glycoalkaloids (BEC) useful for treating cancer (page 221). Cham et al further discloses that rhamnose inhibits the efficacy of BEC and that the aglycone solasodine is not effective against murine S180 (page 221). Thus a person having ordinary skill in the art at the time of the present invention would have been motivated to remove rhamnose and aglycones from the BEC composition in order to improve the efficacy of BEC."

Applicants respectfully traverse the rejection. The conclusion reached by the Examiner in the above paragraph is based on an assumption that the BEC disclosed in Cham is not effective because it contains rhamnose as a degradation product. The Examiner's conclusion is wrong. The rhamnose discussed in the Cham paper is not a degradation product of the BEC in the composition being used but is in fact added to the BEC composition. In support of this position, Applicants invite the Examiner to review page 222 of the Cham paper under the **Materials and Methods** section, where it is clearly shown that the rhamnose being referred to was added to the standard mixture of BEC:

> …A standard mixture of solasodine glycosides (BEC) was dissolved in dimethylsulfoxide (DMSO) at a concentration of 0.5 g BEC/100 ml DMSO. ***Similar solutions were made up but also contained 0.3125, 0.625, 0.9375 g rhamnose.*** These solutions were administered i.p. in concentrations of 8 mg/kg weight for BEC without and with 5 mg, 10mg and 15 mg rhamnose/kg animal."

Cham et al went on to show that "[w]hen four doses of BEC at 8 mg/kg were given on consecutive days . . . all animals survived. . . . The number of survivals was decreased with increasing concentrations of rhamnose." (see page 222, second column).

Importantly, the Cham paper showed that administration of the BEC formulation resulted in survival of ***all animals treated***. The rhamnose taught in the Cham paper was not from the degradation of the BEC composition, but was exogenously added. Given that Cham teaches that the BEC composition (without the addition of exogenous rhamnose) is effective at ensuring survival of all the tested animals, there is no reason why a skilled person would attempt to further purify BEC. The teachings of Cham only stretch to teaching that it is undesirable to ***add*** rhamnose to the BEC composition, Cham et al says nothing about the BEC composition itself being ineffective.

This is entirely different from what is taught in the present application. In the present application it is taught that degradation of BEC leads to accumulation of rhamnose and other sugars and that this accumulation makes the BEC composition less effective as a therapeutic agent. Hence, the present application, for the first time, presents the desirability of further purifying BEC glycoalkaloid compositions to remove essentially all the free sugars that appear in the composition as a result of glycoalkaloid degradation.

In order to clarify this, the methods claims presented herein have specifically been amended to more expressly recite that the methods are for preparing a glycoalkaloid preparation that is substantially free of sugars resulting the degradation of a crystalline or semi-crystalline glycoalkaloid in the preparation.

Applicants submit that in view of this amendment to claims 24 and 43 clearly distinguishes the claimed invention over the disclosure of Cham et al. The secondary references add nothing to the disclosure of Cham et al that would render obvious the claims as currently amended. For example, Gatti et al. (US Patent No. 5,124,318) merely discloses liquid carriers (DMSO, acetic acid or lactic acid) or stabilizing agents to make injectable compositions. The disclosure of Gatti provides nothing regarding the

desirability of removing BEC degradation products. As such, the combination of Cham et al with Gatti et al does not render obvious claims 40, 41, 61 and 62.

Claims 30, 31, 51 and 52 were rejected over a combination of Cham et al in view of Daniels et al (US Patent No. 4,053,591). In making this rejection, the Examiner asserts that Cham teaches that "aclycone solasodine is not effective against murine S189. Thus a person . . . would have been motivated to remove aglycones from the composition disclosed by Cham et al." Applicants respectfully traverse the rejection. Initially, it is noted that these claims depend from claim 24 which applicants believe is distinguished and patentable over Cham and these dependent claims also should be deemed patentable for the same reasons as presented for claim 24. Moreover, Cham et al specifically notes that "solasodine is relatively non-toxic in mice." Given that Cham teaches that solasodine is not toxic and has no effect, the skilled artisan would not be motivated to remove solasodine from the BEC mixture of Cham et al. Further, there is no suggestion anywhere in either Cham or Daniels that solasodine should be removed from a glycoalkaloid preparation. As such, Applicants respectfully submit claims 30, 31, 51 and 52 are not rendered obvious by the combination of Cham et al and Daniels et al.

In view of the above discussion and described amendments, Applicants believe that claims 24-66 are non-obvious over the disclosure of Cham et al either alone or in combination with any of the secondary references and the Applicants respectfully request that the rejections be withdrawn.

2. Rejection of Claims 32-42, 54-58, 60, 65 and 66 under 35 U.S.C. §102(b)

Claims 32-42, 54-58, 60, 65 and 66 were rejected under 35 U.S.C. §102(b). While applicants traverse this rejection, Applicants have cancelled these claims from the instant application in order to progress the prosecution of the instant application.

D. Remarks relating to Guerrero et al.

The Examiner made remarks in response to Applicants previously submitted response to a rejection based on Guerrero. However, while the Examiner states that the remarks are not persuasive, there is no explicit indication if any or which of the claims have been rejected over Guerrero. Therefore, it is not clear whether the rejections based

on Guerrero are being maintained or not. Nevertheless, Applicants are providing the following additional clarifying remarks that show that the invention as claimed is non-obvious over Guerrero.

As noted previously, the methods described herein relate to the washing and removal of free sugar degradation products from a crystalline or semi-crystalline glycoalkaloid preparation. The Guerrero disclosure is related to a process of recovering a solasodine (i.e., the aglycone) composition from a glycoalkaloid solution. The Guerrero disclosure is a multi-step process that involves extraction of the aglycone from an alcohol solution of a crude fruit extract. There is no discussion in Guerrero that an isolated crystalline glycoalkaloid preparation will require further purification to remove degradation products from the glycoalkaloid preparation. In the absence of such a suggestion in Guerrero cannot render obvious the claims of the present invention. As such, Applicants believe that the claims of the invention which relate to methods of removal of degradation products of purified crystalline or semi-crystalline glycoalkaloid preparations are non-obvious over the disclosure of Guerrero.

Respectfully Submitted,

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